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Review

# Protein adsorption onto nanomaterials for the development of biosensors and analytical devices: A review

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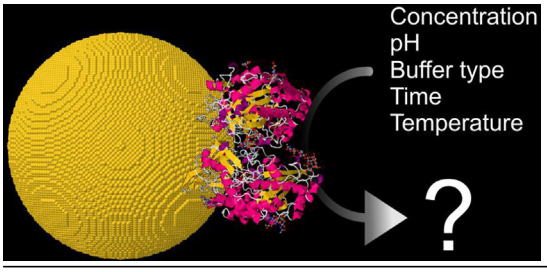
## HIGHLIGHTS

- Articles related to the adsorption of proteins to nanomaterials are reviewed.
- Examples from the last 10 years are discussed focused on biosensors.
- Article includes general information about the proteins and emerging trends.

## GRAPHICAL ABSTRACT

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## ABSTRACT

An important consideration for the development of biosensors is the adsorption of the biorecognition element to the surface of a substrate. As the first step in the immobilization process, adsorption affects most immobilization routes and much attention is given into the research of this process to maximize the overall activity of the biosensor. The use of nanomaterials, specifically nanoparticles and nanostructured films, offers advantageous properties that can be fine-tuned to maximize interactions with specific proteins to maximize activity, minimize structural changes, and enhance the catalytic step. In the biosensor field, protein–nanomaterial interactions are an emerging trend that span across many disciplines. This review addresses recent publications about the proteins most frequently used, their most relevant characteristics, and the conditions required to adsorb them to nanomaterials. When relevant and available, subsequent analytical figures of merits are discussed for selected biosensors. The general trend amongst the research papers allows concluding that the use of nanomaterials has already provided significant improvements in the analytical performance of many biosensors and that this research field will continue to grow.



**Contents**



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**Samir A. Bhakta** graduated from the University of Texas at Austin with a BS in Chemistry in 2007. He was hired by a small environmental lab and specialized in the analysis of metals. After three years, he was admitted to University of Texas at San Antonio as a master's graduate student and soon after to the Ph.D. program. He is currently a Ph.D. candidate in the chemistry program at UTSA and his goals include the design, operation, and application of analytical techniques and biosensors.

**Elizabeth Evans** graduated from Houston Baptist University with a BS in Chemistry in 2012. She is currently a Ph.D. candidate in the chemistry program at the University of Texas at San Antonio. Her current research focuses on the rational development and characterization of microfluidic paper-based analytical devices and biosensors.

**Tomás E. Benavidez** graduated with a BS in Biochemistry (2004) and a Ph.D. in Chemistry (2010) from the National University of Cordoba, Argentina under the supervision of Dr. Baruzzi. After a visit with Dr. Schmickler and Dr. Santos at Universität Ulm (Germany), Dr. Benavidez joined UTSA to investigate the effect of potential applied during the adsorption of macromolecules to different nanostructured films.

**Carlos D. Garcia** received his BS in Biochemistry and Ph.D. in Chemistry from the National University of Cordoba (Argentina) in 1996 and 2001, respectively. Then he performed postdoctoral studies at MSU and CSU under the supervision of Dr. W. Wilson and Dr. Charles Henry, respectively. In 2004, he joined the University of Texas at San Antonio as an Assistant Professor of Analytical Chemistry, where he was promoted to Associate Professor (2010) and to Professor (2014). Currently, his group is focused on the analytical applications of proteins adsorbed to nanostructured surfaces, the advance of microfluidic devices, and the development of instrumentation.

## 1. Introduction

The adsorption of proteins to surfaces is a central concern for the rational design and application of materials [1]. As it will be later specifically addressed, the rate and strengths of the initial physical interactions between proteins and surfaces dictate (to a large degree) the final conformation, stability, and activity of such proteins. This issue, that plays a major role in determining the biocompatibility of materials [2,3], can also dictate the analytical performance of almost every analytical device that uses a biorecognition element (antigen, antibody, enzyme, nucleic acids, or even whole cells) [4]. The topic has become even more relevant in the last decade because an increasing number of applications of biosensors and other protein-based analytical devices have been presented, spanning across a wide array of applications including healthcare, security, environmental, agriculture, food control, process control, and microbiology [5,6]. Most modern biosensors are inexpensive, simple to operate, fast, and selective enough to be applied in the analysis of relatively complex samples. However, and despite the body of research currently available, only a few biosensors are commercially available and can compete with more complex techniques in terms of sensitivity and limits of detection. Aiming to address these shortcomings, a series of strategies have been recently proposed [7–10]. Among those, and reflecting on the progress made in the techniques available for their synthesis and characterization, the use of nanomaterials (defined as materials with at least one feature or component having dimensions between 1 nm and 100 nm) has emerged as one of the leading trends for the development of biosensors and other bioanalytical devices [11]. Their unique chemical, mechanical, electrical, and structural properties enable tuning protein interactions at the nanoscale and catering for the most suitable conditions for immobilization.

In general, and looking beyond the boundaries imposed by the selected transduction method (electrochemical, electrical, optical, piezoelectric, or thermal), assessing the role of the chemistry and topography of the surface [12–14], the physical and chemical characteristics of the protein to be used [15,16], the immobilization route, and the experimental conditions selected for the coupling are fundamental to overcome current limitations. Considering these aspects, researchers currently have a variety of immobilization methods at their disposal [17–19], including covalent attachment, entrapment, encapsulation and cross-linking. While covalent attachment can provide an avenue to form a permanent bond between the functional groups of the protein and those of the substrate, the reactions are typically slow, laborious, and the